## REMARKS

Claims 23-42 are pending. Claims 38-42 are withdrawn from consideration. Claims 25, 26, 30, 33 and 36 are amended. The amendments to the claims are discussed below.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

### I. Election and Restriction

The Election and Restriction requirement is maintained. The Examiner asserts that Applicants arguments are not found persuasive because:

> the Bacillus licheniformis alpha-amylase taught in the reference is known to have useful maltogenic properties as taught by Vickers et al., June 1995, Journal of the Institute of Brewing, Vol. 102, No. 2, pp. 75-78 (see IDS); see entire Abstract and Conclusion; and because WO 91/14772 reference does teach the usefulness of such sequences in transformed cereal plants.

Although Applicants do not hereby traverse the Election/Restriction. Applicants must, however, clarify the record, namely, by pointing out that the Examiner's statements are factually incorrect as they are based on a case of mistaken identity. In particular, the Examiner is mistakenly confusing the enzyme of Vickers et al., which is an alpha-amylase (1,4, alpha-D-glucan gluanohydrolase) with the very different enzyme involved in the present invention, namely, a maltogenic alpha-amylase (glucan 1,4, alpha-maltohydrolase). Alpha-amylases and maltogenic alpha-amylases are different enzymes having different activities and different enzymatic classifications. Indeed, Vickers et al. discloses a *Bacillus licheniformis* alpha-amylase not a *Bacillus licheniformis* maltogenic alpha-amylase. Similarly, the alpha-amylases mentioned in WO 91/14772 are alpha-amylases not maltogenic alpha-amylases. Thus, a *Bacillus licheniformis* alpha-amylase is not known to have the properties of the different enzyme, i.e., a maltogenic alpha-amylase.

This point is also discussed in respect to the prior art rejections, which are also based on a case of mistaken identity.

**II. The Rejection of Claims 23-37 under 35 U.S.C. 112**

Claims 23-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This rejection is respectfully traversed.

The specification discloses transgenic cereal plants cells comprising nucleotide sequences encoding maltogenic alpha-amylases, including maltogenic alpha-amylases which have the amino acid sequence of SEQ ID NO:2 (claim 25), including maltogenic alpha-amylase having at least 70% identity to SEQ ID NO:2.

Foremost, Applicants are puzzled as to how claim 25 can be included in the rejection given the Examiner's specific acknowledgement that the amino acid sequence of SEQ ID NO:1 and SEQ ID NO:2 are described, and plant cells and plants transformed therewith. In particular, the Examiner acknowledges that:

> Applicant describes SEQ ID NO:1 encoding SEQ ID NO:2, and
> plant cells and plants transformed therewith.

The Examiner's statements clearly confirm the written description support for claim 25. Indeed, claim 25 is directed to the very subject matter the Examiner acknowledges is described by Applicants.

With respect to transgenic cereal plants cells comprising nucleotide sequences encoding maltogenic alpha-amylases "having at least 70% identity to SEQ ID NO:2" (claim 26), this subject matter is also clearly described in the specification. In particular, an artisan would reasonably conclude that applicants were in possession of transgenic cereal plants comprising nucleotide sequence encoding not only the maltogenic alpha-amylases of SEQ ID NO:2, but also of transgenic plants comprising nucleotide sequences encoding maltogenic alpha-amylases having a very high degree of structural relatedness to SEQ ID NO:2, including, an amino acid sequence which is at least 70% identity to SEQ ID NO:2. In this regard, Applicants disclose, beginning on page 7 at line 5 to page 10, line 35, numerous maltogenic alpha amylases in addition to the maltogenic alpha-amylases of SEQ ID NO:2 which are at least 70% identical to SEQ ID NO:2. Thus, an artisan would reasonably conclude that Applicants were in possession of the subject matter of claim 26.

An artisan would also reasonably conclude that Applicants were in possession of transgenic plant cells encoding maltogenic alpha-amylases in general. The Examiner contends that Applicants do not describe "any DNA or amino acid sequences other than SEQ ID NO:1 and

2 or plant and plants transformed herewith." This is not correct. As previously stated, Applicants disclose, beginning on page 7, line 5 to page 10, line 35, numerous maltogenic alpha amylases.

The Examiner subsequently refers to these maltogenic alpha-amylase variants described on page 7, line 5 to page 10, line 35 as "hypothetical substitutions." This statement is also clearly not correct as these substitutions are not "hypothetical". In this regard, Applicants direct the Examiner to the examples of U.S. Patent 6,162,628, which describe that many of the variants disclosed on page 7, line 5 to page 10, line 35 were, in fact, made.

Accordingly, under *Univ. of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), the proper conclusion is that the claims have sufficient written description support such that the skilled artisan would conclude that, at the time the application was filed, the inventors had possession of the claimed invention.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

**III. The Rejection of Claims 23-37 under 35 U.S.C. 112**

Claims 23-37 are rejected under 35 U.S.C. 112, as allegedly lacking enablement. The Examiner states:

> Applicant broadly claims a nucleotide sequence encoding a maltogenic alpha-amylase; a maltogenic alpha amylase derived from a microorganism; a maltogenic alpha amylase having the amino acid sequence of SEQ ID NO:2, a maltogenic alpha-amylase having amino acid sequence 1-686 of the amino acid sequence encoded by SEQ ID NO:1; a maltogenic alpha-amylase having an amino acid sequence having at least 70% sequence identity to SEQ ID NO:2; a maltogenic alpha-amylase having an amino acid sequence having at least 70% sequence identity to amino acid sequence 1-686 encoded by SEQ ID NO:1; transgenic cereal cells and plants thereof; and seeds comprising said sequences encoding an alpha-amylase in an amount effective to delay staling of bread baked from the seed.
>
> Applicants teaches SEQ ID NO:1 and 2; hypothetical amino acid

substitutions to the polypeptide of SEQ ID NO:2 from maltogenic alpha amylase variants disclosed in WO 99/43794 (specification pages 6-10); and prophetic biolistic transformation of wheat (Example 1 pages 21-24), and a proposed construction of a construct comprising 'Novamyl (SEQ ID NO:1) maltogenic alpha amylase transformed into wheat protoplast cells and regenerated into mature wheat plants.

The Examiner then provides an argument that a skilled artisan would not be able to obtain the "claimed variants of SEQ ID NO:1 and 2 comprising any other maltogenic alpha amylase." The Examiner further provides arguments of the difficulties of predicting enzyme activity of variants.

Furthermore, the Examiner asserts that it is unpredictable to change the phenotype of a plant when attempting to modify metabolism, citing Sweetlove L. et al. Biochem J. 1996, where it is alleged that "the overexpression in potatoes of an ADP glucose pyrophophoryase gene from E. coli wherein increased activity resulted in an increased flux into the starch pathway but also resulted in an increase in the capacity of the tubers to degrade the starch in a manner proportionate to increased flux."

This rejection is respectfully traversed. Foremost, Applicants disagree with the Examiner's characterization of what is being claimed. Applicants are **not**, as alleged by the Examiner, broadly claiming a nucleotide sequence encoding a maltogenic alpha-amylase; a maltogenic alpha-amylase, a maltogenic alpha-amylase having the amino acid sequence of SEQ ID NO:2 or SEQ I DNO:1 and related sequence. The claims are instead clearly directed to transgenic cereal plant cells.

In association with the mischaracterization of the claimed invention, the Examiner presents arguments for how one skilled in the art would allegedly not be able to prepare the claimed variants. Applicants are not, however, claiming variants. Nevertheless, the variants, which the Examiner incorrectly describes as "hypothetical substitutions", can be made or obtained by the artisan without undue experimentation. See, e.g., the examples of U.S. Patent 6,162,628, which describes that many of the variants disclosed on page 7, line 5 to page 10, line 35, were, in fact, made.

With respect to the claimed subject, i.e., transgenic cereal plant cells, Applicants respectfully submit that the claims are enabled. Again, Applicants question how claim 25 is

possibly included in the enablement rejection. As discussed above, the Examiner has acknowledged that Applicants have described the amino acid sequence of SEQ ID NO:1 and SEQ ID NO:2 as well as plant cells and plants transformed herewith. Applicants also provide detailed guidance of how the artisan can prepare the transgenic plants of the invention, including, cloning (page 12, line 30 to page 14); sources of such maltogenic alpha-amylases (page 6, line 11 to page 10, line 35); preparing expression constructs (page 14, line 8 to page 16, line 7 and Example 1 and Example 2); selecting suitable transgenic plant species (page 6, lines 9-23); and transforming the plants (page 16, line 35 to page 17, line 33 and Example 1 and Example 2). Thus, claim 25 is clearly enabled.

The remaining claims are also clearly enabled. Claim 1 is directed to a transgenic cereal plant cell comprising a nucleotide sequence encoding a maltogenic alpha-amylase. Once apprised of the claimed invention, and based on the very detailed guidance provided in the specification, it would be routine for the highly skilled artisan to make a transgenic cereal plant comprising a nucleotide sequence encoding a maltogenic alpha-amylase (including transgenic plant cells comprising nucleotide sequences encoding maltogenic alpha-amylases, and more preferably maltogenic alpha-amylases "having at least 70% identity to SEQ ID NO:2" (claim 26). Indeed, the specification provides detailed guidance of how the artisan can prepare the transgenic plants of the invention, including

- cloning a DNA sequence encoding a maltogenic alpha-amylase (page 12, line 30 to page 14); including sources of such maltogenic alpha-amylase in addition to SEQ ID NO:1 and 2 (page 6, line 11 to page 10, line 35);
- preparing expression constructs (page 14, line 8 to page 16, line 7 and Example 1 and Example 2);
- selecting suitable transgenic plant species (page 6, lines 9-23); and
- transforming the plants (page 16, line 35 to page 17, line 33 and Example 1 and Example 2).

Sweetlove et al. Biochem J. 1996, which is cited by the Examiner for the alleged unpredictability of the claimed invention, is not seen to establish this point. The Examiner is apparently associating the mutant tuber plants of Sweetlove et al., which have increased amounts of a wild-type gene, with the transgenic plants of the present invention, which have a non-endogenous gene inserted in them. The Examiner appears to imply because Sweetlove et al.

reports that there was not a major increase in the amount of starch (i.e., the rate of starch synthesis), this shows the unpredictability of the claimed invention.

Notwithstanding that the problems presented in Sweetlove et al. are not the same as those addressed by the present invention, Sweetlove et al. is clearly not relevant to the claimed invention for another fundamental reasons. In particular, although Sweetlove's teaching of the amount of enzyme produced by the transgenic plants may have relevance to what particular application the transgenic plants can be used for (e.g., is the enzyme produced in a sufficient amount for the particular application), it does not, however, stand for the proposition that an artisan cannot make the transgenic plants that produce a maltogenic alpha amylase.

Indeed, if Sweetlove et al. is believed by the Examiner to be relevant to enablement of the claimed invention, it actually supports that the claimed invention is enabled. That is, although Sweetlove et al. teach that "a major increase in the rate of starch synthesis does not necessarily lead to an increase in starch content," Sweetlove et al. also specifically teach that although "increasing the activity of ADPglucose pyrophophorylase did not increase the starch content of the tubers in our work, direct assessment of the movement of 14C from [14C]sucrose into starch very strongly suggests that the rate of starch synthesis was increased." See Sweetlove et al. at page 497, col. 2. Thus, Sweetlove et al. is not a failed experiment, but a success. Indeed, the authors were able to successfully change the genetic make-up of the plant cells to increase the activity of the enzyme.

Finally, with regard to the Examiner's statement that undue experimentation is required. Applicants respectfully disagree. Applicants acknowledge that there may be some *routine* experimentation involved in the claimed invention, however, the test for enablement is not whether *any* experimentation is required, but rather whether *undue* experimentation is required. Indeed, as noted by the *In re Wands* court (*In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), the test for determining whether undue experimentation is required even permits a considerable amount of testing. The type experimentation that would be required in practicing the present invention is experimentation that is *routinely* encountered and performed when preparing transgenic organisms (see many of the references relied upon by the Examiner), e.g., finding a promoter that gives an suitable expression in the host or preparing the vector, e.g., a plasmid. Thus, the experimentation that would be required by the present invention is clearly not undue, and even if the experimentation involved might be time consuming, it is the *nature* and not the *amount* of experimentation that is determinative of non-enablement. *See Hybritech v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986).

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

**IV. The Rejection of Claims 25-26, 30, 33 and 36 under 35 U.S.C. 112**

Claims 25-26, 30, 33 and 36 are rejected under 35 U.S.C. 112, as indefinite. This rejection is respectfully traversed.

Claims 25, 26, 33, and 36 are rejected as referring to the amino acid of SEQ ID NO:1, whereas the Examiner notes that SEQ ID NO:1 is a polynucleotide. Although SEQ ID NO:1 does recite a polynucleotide, it also recites an amino acid sequence. Nevertheless, to expedite prosecution, the claims have been amended to reference the mature peptide of SEQ ID NO:2 (namely, amino acids 34-719).

Claim 30 is rejected as employing an improper Markush terminology in recitation in line 1 and 2 of "plant cell of Claim 35 and progeny. The Examiner states that replacement of "and" with "or" in line 1 would obviate this rejection. Applicants have adopted the Examiner's suggestion for obviating the rejection.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

**V. The Rejection of Claims 23-24, 27, 30-32, 34-35 and 37 under 35 U.S.C. 102 (Ooyen et al. in light of Vickers et al.)**

Claims 23-24, 27, 30-32, 34-35 and 37 are rejected under 35 U.S.C. 102 as being anticipated by Van Ooyen et al. (US Pat. 5,705,375) in light of Vickers et al., 1995). This rejection is respectfully traversed.

Van Ooyen et al. do not teach a maltogenic alpha-amylase. Van Ooyen et al. teach an alpha-amylase. Thus, the Examiner rejections is based on a case of mistaken identity as an alpha-amylase is NOT a maltogenic alpha-amylase. Indeed, the enzymes are structurally and functionally different, and are accordingly classified under different Enzyme Classification (EC) numbers (compare EC 3.2.1.1 for the alpha-amylase classification) to, e.g., EC 3.2.1.133 (an example of maltogenic alpha-amylase classification). Thus, the *Bacillus licheniformis* alpha-amylase of Van Ooyen et al. is an alpha-amylase not a maltogenic alpha-amylase.

Moreover, Vickers et al. does not disclose that *Bacillus licheniformis* alpha-amylase is inherently a maltogenic alpha amylase. Indeed, Vickers et al. is describing an "alpha-amylase"

and an alpha-amylase cannot "inherently" be a different enzyme, i.e., a maltogenic alpha-amylase.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102 as the referenced cited by the Examiner do not teach maltogenic alpha-amylases. Applicants respectfully request reconsideration and withdrawal of the rejection.

**VI. The Rejection of Claims 23-24, 27, 30-32, 34-35 and 37 under 35 U.S.C. 102 (Ooyen Barro et al.)**

Claims 23-24, 27, 30-32, 34-35 and 37 are rejected under 35 U.S.C. 102 as being anticipated by Barro et al. This rejection is respectfully traversed.

This rejection appears to rely on wheat containing "endogenous maltogenic alpha-amylase." However, Barro et al. do not teach that wheat plants contain endogenous maltogenic alpha-amylases. Indeed, the maltogenic alpha-amylases known in the art are derived from microorganisms, and Applicants are not aware of any plant, including, wheat, which has endogenous maltogenic alpha-amylases. Accordingly, Barro et al. is not relevant to the claimed invention.

In this regard, the present invention is directed to transgenic cereal plants which have genes which are not known to be endogenous to cereal plant, namely, genes encoding maltogenic alpha-amylase. To the best of Applicants' knowledge, this has not been described or suggested in the prior art.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

**VII. The Rejection of Claims 23-24, 27-28, 30-32, 34-35 and 37 under 35 U.S.C. 103 (Pen et al. in view of Barro et al.)**

Claims 23-24, 27-28, 30-32, 34-35 and 37 are rejected under 35 U.S.C. 103 as being unpatentable over Pen J., WO 91/14772 in view of Barro et al. The Examiner states that:

> Applicant broadly claims a nucleotide sequence encoding a maltogenic alpha-amylase; a maltogenic alpha amylase derived from a microorganism; a maltogenic alpha amylase having the amino acid sequence of SEQ ID NO:2, a maltogenic alpha-amylase having amino acid sequence 1-686 of the amino acid sequence encoded by SEQ ID NO:1; a maltogenic alpha-amylase

> having an amino acid sequence having at least 70% sequence identity to SEQ ID NO:2; a maltogenic alpha-amylase having an amino acid sequence having at least 70% sequence identity to amino acid sequence 1-686 encoded by SEQ ID NO:1; transgenic cereal cells and plants thereof; and seeds comprising said sequences encoding an alpha-amylase in an amount effective to delay staling of bread baked from the seed.

As discussed above, this characterization of the claimed invention is not correct. Applicants are not, as alleged by the Examiner, broadly claiming a nucleotide sequence encoding a maltogenic alpha-amylase; a maltogenic alpha-amylase, a maltogenic alpha-amylase having the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:1 and related sequence. The claims are instead directed to transgenic cereal plant cells.

With respect to the prior art asserted, Pen et al. does not teach expression of a maltogenic alpha amylase gene at commercially acceptable levels in tobacco. Rather, Pen et al. is also clearly directed to alpha-amylases not the different enzymes maltogenic alpha-amylases.

Barro et al., as previously discussed, is clearly irrelevant to the claimed invention, as, among other things, Barro et al. does not teach that plants encode endogenous maltogenic alpha-amylase.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103. Applicants respectfully request reconsideration and withdrawal of the rejection.

**VIII. The Rejection of Claims 23-37 under 35 U.S.C. 103 (Pen et al. in view of Barro et al. in view of Accession number P19531, Diderichsen et al. and Christophersen et al.)**

Claims 23-37 are rejected under 35 U.S.C. 103 as being unpatentable over Pen et al. in view of Barro et al. in view of Accession number P19531, Diderichsen et al. and Christophersen et al. The Examiner states that:

> Applicant broadly claims a nucleotide sequence encoding a maltogenic alpha-amylase; a maltogenic alpha amylase derived from a microorganism; a maltogenic alpha amylase having the amino acid sequence of SEQ ID NO:2, a maltogenic alpha-amylase having amino acid sequence 1-686 of the amino acid sequence encoded by SEQ ID NO:1; a maltogenic alpha-amylase having an amino acid sequence having at least 70% sequence

identity to SEQ ID NO:2; a maltogenic alpha-amylase having an amino acid sequence having at least 70% sequence identity to amino acid sequence 1-686 encoded by SEQ ID NO:1; transgenic cereal cells and plants thereof; and seeds comprising said sequences encoding an alpha-amylase in an amount effective to delay staling of bread baked from the seed.

Again, it is noted that Applicants are not, as alleged by the Examiner, broadly claiming a nucleotide sequence encoding a maltogenic alpha-amylase; a maltogenic alpha-amylase, a maltogenic alpha-amylase having the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:1 and related sequence. The claims are directed to transgenic cereal plant cells.

Pen et al. and Barro et al. are discussed above. The Examiner states that Pen and Barro do not teach a maltogenic alpha amylase having at least 70% sequence identity to SEQ ID NO:2 or 70% sequence identity to the amino acid sequence encoded by SEQ ID NO:1 isolated from Bacillus train NCIB. The Examiner states, however, that it would be obvious to substitute the enzymes of Accession number P19531, Diderichsen et al. and Christophersen et al. for the enzymes of Pen and Barro et al.

With respect to Pen et al., there is no teaching or suggestion in Pen et al. any of the other cited references to substitute a maltogenic alpha-amylase of Accession number P19531, Diderichsen et al. and Christophersen et al. for an alpha-amylase of Pen et al. Indeed, the enzymes have different activities, and thus, an artisan would not be motivated to make this substitution.

With respect to Barro et al., it is clearly not relevant to the claimed invention, as, among other things, Barro et al. do not teach that plants encode endogenous maltogenic alpha-amylases.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103. Applicants respectfully request reconsideration and withdrawal of the rejection.

## IX. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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